understood. Claims 1-62 were rejected under 35 U.S.C. 112 first paragraph. Claims 1-56 were rejected under 35 U.S.C. 112 second paragraph. Claims 1,2,9, 10 and 11 were rejected under 35 U.S.C. 102(e) over Ivory, et al. These rejections are addressed by the discussion below.

Claims 1-62 were originally presented. Claims 1-62 remain in the application. No claims have been canceled. No claims have been added.

1. Drawing Objections

The drawings were objected to under 37 C.F.R. § 1.83(a) for not showing every feature of the invention specified in the claims. The objections are not entirely understood, as set forth below. As far as applicant can understand the objections, Applicant has attempted to explain the reason(s) the objections as understood should be withdrawn and/or has acknowledged possible valid bases for objection and has tried to amend the case to address the concern(s). For example, as shown on the enclosed drawing replacement sheets, Figure 5 has been amended without adding new matter. Commensurate amendments to the specification have also been made.

The Examiner's objections to the drawings as not explicitly showing "packing" is not entirely understood. Applicant reminds the Examiner that this is well known in the art, and does not really admit of a drawing. For example the cited Ivory reference, which the Examiner assisted in examining, does not have a figure which explicitly shows the packing, though it is claimed (*e.g.* in claim 5) of the Ivory reference.

Nevertheless, Applicant has amended the specification and drawing figures to add a reference number regarding packing, to address the concern raised as far as understood.

However, it appears that the best that can be done is to indicate the channel where the packing would be. This could be more confusing than helpful.

Nevertheless the Applicant thanks the Examiner for pointing out that clarity might be improved by provision of a reference number to the location of packing, if that is the burden of the rejection. The attached replacement sheet of drawings includes changes to FIG. 5 comprising adding a reference number (67) to the location of packing which, as explained in the specification, in one embodiment can fill the channel 60. Since packing is well known, detailed illustration is not believed required, as discussed further below, and indication of its location and its extent, commensurate with the channel, is deemed sufficient, being at least equivalent to a labeled box (per 1.83(a)) in three dimensions., A drawing symbol could be added if the Examiner both requires it and can suggest one appropriate to the usage.

The attached replacement drawing sheet, which includes FIG. 5 replaces the original sheet containing FIG.5. If the Examiner believes the amendment is helpful, the change can be retained. If the Examiner feels, after reviewing the drawings, that it may be more confusing than helpful, applicant would be willing to revert to the original drawing figure. The replacement specification paragraph set forth above, from page 17, beginning at line 19, includes a repetition of language copied directly from p. 10 of the specification, and a reference number "67" has been inserted after the word "packing."

No new matter has been added by adding the reference number since the application as filed discusses the element and its location at least at p. 10, as well as in claims 6 and 32, as has been pointed out by the Examiner. Applicant hopes these amendments will address the concerns raised, and requests the objection concerning this element be withdrawn in light of said amendments. If Applicant has misunderstood the basis of the rejection, clarification is

requested.

Regarding another concerned raised, the filament and field generator elements are shown in the drawings in compliance with 37 CFR 1.83(a) and applicable Sections of the MPEP. The objections citing their omission are not understood, as will be further discussed below.

Regarding another concern raised, the elements comprising the first and second orientation electric field generators, as set forth in the specification, are shown. See, *e.g.* pp. 23 and 29 of the specification and the drawing figures referenced thereby. Each element comprising the field generators is described, referenced, and shown in the drawing figures. Since they comprise disparate elements at disparate locations, a single reference number to a orientation electric field generator would perhaps be more confusing than clarifying; for example, appearing to reference the whole device, or an inconsistent reference to multiple elements already referenced by different reference numbers. If the Examiner can suggest an improvement in this regard applicant would be happy to attempt to render an improvement by adding a reference number and the multiple leaders that would be required for each generator, for example. However, applicant submits that the requirements of Section 1.83(a) have been met.

Concerning the objection raised about showing a filamentary element including a continuously varying resistor, the Examiner is respectfully directed to the specification at pp. 17-18 and drawing figure 5 referenced thereby. These set forth this element of the claims. The Examiner's contention that such a filament is not shown in the drawings is not understood. Applicant requests that the objections be clarified or be withdrawn.

Materials properties changing as a function of position does not necessarily admit of being shown in a drawing. Gray scale, for example, is not currently allowed. If the Examiner could suggest how this limitation admits of illustration and how it could be illustrated, applicant would be grateful. However, it is submitted that those skilled in the art will appreciate that the element, made of the material as described in the specification, is shown; and that they will further appreciate that the composition or some attribute of the material can change with position along its length in one or more directions without necessarily illustrating this molecule by molecule, or pore size by pore size, etc. since that would not be discernable (except perhaps by color, or grayscale, for example) anyway. The Examiner is respectfully reminded that the physical element is shown; and, as far as illustrating the materials properties are concerned, it would be well to recall that drawings are not necessarily required in chemical cases for good reason. Whether the element is a resistive filament contour resistor, laterally extending contour resistor element, or packing with varying resistance (to name some examples) it is submitted that the physical element, as far as it admits of a drawing and can be shown in the drawings, is shown. Moreover, the written description of the construction of the resistor is set forth and in this case meets the statutory requirements of disclosure in support of the claims. The objection must be withdrawn, or Applicant respectfully requests that it be clarified.

Regarding the objection to the drawings in that they show the analyte concentrator as a "black box;" this may be a fair characterization of its depiction in FIG. 3. However, the case as a whole, including FIG. 14 which is devoted entirely to the analyte concentrator, and the discussions of the element at pp. 12, 15, 29, 35, 41, 44-46, leads applicant to question the basis, intent and reasoning of the objection. The objection as stated must be withdrawn, or

must be further explained, in light of the foregoing; for applicant is unable to formulate a response based upon guessed-at theories of the basis of the rejection.

2. Section 112 Rejections

These rejections are not understood, and appear at least to some extent to be a result of a failure of the Examiner to appreciate the salient principles, known to those with a background in electrical engineering and device fabrication, which underlie the presentation of the subject matter. Nevertheless, so as to fully respond to the Examiner's rejections, insofar as applicant can, under the circumstances, understand the Examiner's concerns, the bases of rejection of each claim specifically mentioned by the Examiner will be addressed in turn.

Claim Rejections - 35 U.S.C. § 112, First Paragraph

I. Concerning "pumps"

Claims 59 and 62 stand rejected under § 112, first paragraph, as containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, that "the specification...does not support use of a pump to balance the force produced by the continuous electric [field] intensity generator" (p.3 para.2 of the Office Action).

This rejection is not understood. It is disclosed in the application to use a pump to provide a counter-force to electrophoretic migration (see, e.g. p. 5 lines 10-13, and p. 5 line 20 to p. 6 line 4). This is known in the art, as the specification teaches. Applicant has

provided an example of a pump in the detailed description, specifically the electroosmotic bulk flow generator disclosed, which is the best mode known to applicant at the time of filing of the application. However, a "pump" can be any of the known types of pumps known in the art for providing flows suitable for the application. Syringe pumps, for example, are widely known and commercially available, and are commonly used. Since a pump is understood, both in the art and, in fact, in general usage, to be essentially any apparatus which impels, drives, compresses, raises, pressurizes, etc. a fluid, it is respectfully submitted that an example of such an apparatus is disclosed. Moreover, inducing electroosmotic flow (EOF) as the "pump" is known and understood in the art. The Examiner is respectfully directed to the Ivory reference he has cited, and which the Examiner assisted in examining, at col. 17, line 54 and col. 20 lines 28-33. For at least these reasons, Applicant is unable to understand the basis, reasoning, and intent of the rejection, and requests that the rejection be withdrawn or explained.

II. Concerning linguistic issues:

Claims 1-62 stand rejected under § 112, first paragraph, as "containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed had possession of the claimed invention" (p. 3 Para. 3). Specifically, that:

> "The specification is replete with defects such as terms, which are not clear, concise, and exact too numerous for the examiner to point out in detail. The following defects are REPRESENTATIVE of the more serious defects. For example the applicant states that using contour electrodes to define a portion of

the separation channel results in a continuous electric field intensity gradient. For example, the specification recites page 30, lines 15 and 16, 'The shape of the contour of the resistors causes the channel voltage gradient to vary in a *predictable manner*.' The applicant fails to provide any guidelines, e.g. design equations, design the contour electrodes to produce a desired voltage gradient. The examiner did a search of USPAT......DERWENT, and CAPLUS, and could find no teaching of the use of contour resistors to create a continuous electric field intensity gradient. Moreover, the examiner could not find even one occurrence of the term "contour resistor". The applicant presents no experimental evidence or theoretical reasoning that contour resistors will produce a continuous electric field intensity gradient."

This rejection is not understood, as those skilled in the relevant art can fully appreciate that at the time the application was filed Applicant had possession of the invention. See Applicant's Declaration (attached), and attached Exhibits thereto. In further response to these concerns, as far as Applicant understands them, the Applicant has several comments in response, to wit:

A. Concerning Patent Application References to "Contour Resistors"

(As a preliminary aside, the term "contour electrode" page 28 line 20 of the specification, as filed, is incorrect and the result of a typographical error, and should read simply "electrode" as set forth in the corrected replacement paragraph set forth above.)

As is well established, a patent applicant can be his own lexicographer. Per Applicant's Declaration, the term has been coined to refer to structure in Applicant's own original invention and embodiments thereof, which previously did not exist, to Applicant's knowledge. The

meaning of the term is defined by the specification. The following descriptions of the contour resistor have been extracted from the patent application as filed, and are representative of the more relevant references to be found therein:

1. Contour resistor location:

   (page 30 lines 8-12) *"A set of distributed contour resistors 46, each 15 cm in length and 12 μm thick, are placed centrally in the channel. The resistors are in the plane of the channel and contact the channel in the 50μm height dimension forming a portion of the wall (12 μm out of 50 μm)...."*

2. Contour resistor electrical definition:

   (page 30 lines 11-12) "*.....cause(s) a resistive shunt to be formed with the electrolyte in the main channel...."*

   (page 30 lines 15-17) "*The shape of the contour of the resistors causes the channel voltage gradient to vary in a predictable manner."*

   (page 30 lines 17-19). "*A constant width resistor has a linear voltage drop per increment of channel distance, while contour resistors cause the voltage drop per increment of channel to vary. The voltage gradient of the electrolyte in the channel can thus be* <u>*contoured*</u> *for any monotonic function*" (emphasis added).

The term "contour resistor" is a descriptive term referring to what the resistor does to the channel voltage.

3. <u>Contour resistor physical definition:</u>

(page 10 lines 1-16) "*A continuously varying resistor in fluid communication with the separation channel along at least a portion of the longitudinal axis intermediate the first and second ends comprises a resistor having a resistance that varies as a continuous function of position along the longitudinal axis of the separation channel, whereby an electric potential in the electrolyte fluid varies as a nonlinear continuous function of position along the longitudinal axis of the separation channel, and as a result the electric field intensity varies as a continuous function of position along the longitudinal axis over at least a portion of the separation channel intermediate the first and second ends. Such a resistor can comprise a contour resistor which contacts the fluid within the channel by forming a part of the channel wall...*"

(page 10 lines 12-16) "*In further detail, a contour resistor can comprise a conductive material having a cross section shape which varies as a continuous function of position along the longitudinal axis.* "

(page 30 lines 12-15) "*Each resistor is geometrically shaped or has varying resistivity with longitudinal length to cause a nonlinear voltage gradient within the channel. If the resistors are shaped, then at the anode side, the distributed resistors are thin, (a high resistance), while at the cathode side the resistors are wide, (a much lower resistance)*"

(page 34 lines 17 – 21) "*...is to apply overlapping geometries of decreasing resistivity inks such that at the cathode end 108 of the contour resistor 46 has a low resistivity and the*

anode end 106 has a high resistivity with a resistivity gradient between the two ends. The precise voltage profile is then achieved by laser trimming the outboard side 110, 112 of the geometries."

(page 31 lines 17 –21, page 32 lines 1-4) *The definition of resistance in relation to mechanical dimensions and resistivity for an electrolyte...* (or for a contour resistor).

$$R = (\rho X)/(WH) \text{ or } \rho = (RWH)/(X)$$

Where R is resistance in ohms, X is channel length in cm, W is channel width in cm and H is channel height in cm and ρ is resistivity in ohm-cm.

4 Mathematical Determination of the incremental resistance of the contour resistor:

(pages 30 – 33) describes mathematically how to determine the incremental resistance of the contour resistor. An example is given using a linear electric field intensity gradient continuum.

(page33 lines 9-13) The incremental resistance of the contour resistor, R_R, is mathematically defined as follows:

$$R_R = (2)(\Delta V)(R_C)/[(I)(R_C) - (\Delta V)]$$

where ΔV is the incremental voltage drop (0.2 cm), R_C is the incremental channel resistance and R_R is the incremental resistance of the contour resistor

5. Drawings that show contour resistors:

(Figure 3) The contour resistor is denoted as item 46.

(Figure 4) The contour resistors are denoted as item 46.

(Figure 6) The contour resistors are denoted as items 74 and 76.

(Figure 7) The cross section of the contour resistors are denoted as items 74 and 76

(Figure 8) A contour resistor is denoted as item 76

(Figure 10) The contour resistors are denoted as item 46 and their outboard sides are denoted as 110 and 112

(Figure 11) The cross section of the contour resistors are denoted as items 74 and 76

(Figure 12) Shows the profile of the incremental resistance of the contour resistor for a linear electric field intensity profile. This graph is the result of the design process described on pages 30- 33.

6. <u>Contour resistor fabrication</u>:

(page 24 lines 15-18) "*...the configuration illustrated is formed by known silk-screen techniques, applying layers in turn on the glass substrates (not shown) which sandwich the configuration within the monolith (not shown).* "

(page 25 lines 18-20) "*The substrates and inks are identical to thick film hybrids...* "

(page 34 line 14 to page 35 line 4) . *A second method is to decrease the incremental resistance of the contour resistor by increasing the thickness of the thick film resistor as it approaches the cathode, but this would require very unusual screening techniques to lay down such a structure. A third method, illustrated in FIG. 10, is to apply overlapping*

geometries of decreasing resistivity inks such that a cathode end 108 of the contour resistor 42 has a low resistivity and the anode end 106 has a high resistivity with a resistivity gradient between the two ends. The precise voltage profile is then achieved by laser trimming the outboard sides 110, 112 of the geometries. A fourth method is to use inkjet technology to deposit the varying resistivity ink directly from three or four ink resistivities, which are applied using a computer controller to produce the desired resistance gradient. This can be followed by laser trimming. This last approach can also limit the width of the contour resistor to less than half a channel width. For limited resistor excursions of less than an octave, single resistivity ink is adequate but would still require laser trimming.

7. <u>Experimental Results Concerning Contour Resistors:</u> The Examiner has questioned the utility/operability of the disclosed invention in conversation with Applicant's representative. In the Letter response (copy attached, with enclosures), submitted in early March of 2003 in response to telephone inquiry by the Examiner to Applicant's representative concerning whether there were experimental results in accordance with the teachings of the application, several examples of contour resistors are shown based on fabrication techniques (screened thick-film inks) that are described in the patent application:

   1. Page 1, Figure 5. Experimental results show a photograph of a section of a channel focusing dyed proteins between contour resistors.

   2. Page 4 shows the outline of contour resistors that create multiple electric field intensity slopes as described mathematically on page 3.

   3. Page 5 graphs the electric field intensity profile derived from measuring incremental channel voltages.

4. Page 6 is a photograph of the substrate that has screened on contour resistors that generate multiple electric field intensity slopes.

Applicant has provided in the disclosure:

- The location of the contour resistors with respect to the channel and the assembly (A.1, above)
- The electrical properties of the contour resistors (A.2)
- The physical description of the contour resistors (A.3)
- A mathematical means of calculating what the incremental voltage of the channel should be for a given electric field intensity gradient and a mathematical expression for the incremental contour resistor value (A.4)
- 8 different drawings showing the contour resistor with respect to other elements of the assembly (A.5)
- Fabrication techniques to make a contour resistor and other elements of the assembly (A.6)
- Now, per the attached letter responding to the Examiner's inquiry, evidence of the functionality of a device in accordance with the teachings of the disclosure, <u>i.e.</u> Experimental results showing the separation of dyed proteins using contour resistors (A.7) are provided to the Office in response to the Examiner's request
- The measurement of a complex electric field intensity profile per the disclosure (A.7)
- A photograph of a substrate with screened contour resistors per the disclosure (A.7)

Applicant is unable to understand and further respond to the Examiner's concerns in light of the foregoing.

However, Applicant will assume for purposes of response that the Examiner objects to the term because he has not heard it before. "Contour resistor" is a descriptive term coined by the applicant to describe the one or more resistors that are electrically in parallel with the electrolyte of the channel and used to modify the resultant electrical properties of the channel to produce a varying electric field intensity profile or "*The voltage gradient of the electrolyte in the channel can thus be* <u>*contoured*</u> *for any monotonic function*" (page 30 lines 18 – 19). This is consistent with the definition of the term coined by applicant. However, it must also be said that the word "contour" has also been used in the patent application to describe the outer (lateral) shape of the resistors that are in parallel with the electrolyte. This has been clarified by this amendment, *i.e.* "*the shape of the contour ~~of the~~ resistors causes the channel voltage gradient to vary in a predictable manner*" (paragraph from page 30 lines 15 – 17, as set forth above).

Other Embodiments of the "contour resistor", however, may instead vary in another parameter, such as thickness or resistivity, and hence may not have a lateral variation in shape. The meaning of contour resistor will be understood by one skilled in the art as a resistor(s) that is in parallel with the electrolyte in the channel to contour a monotonic voltage function. The specification is consistent on this definitional point throughout, both before and after these amendments.

Applicant believes that the use of contour resistors for creating electric field intensity profiles is novel and patentable. Therefore it is to be expected that the patent Examiner <u>should not</u> be able to find any reference to this usage in the literature.

B. Regarding Continuously Varying Resistors:

In the outstanding office action the Examiner goes on to state:

"Similarly, the applicant broadly recites continuously varying resistors comprising one of the following: 1) a filament within the first separation channel, 2) a packing within the first separation that varies in resistivity as a continuous function of position along the longitudinal axis, 3) a conductive material having a cross section shape which varies as a continuous function of position along the longitudinal axis, 4) a contour resistor has a material property that varies as a continuous function of position along said longitudinal axis. The written description of the invention provides no design or fabrication details of any of these resistors and none of these resistors is illustrated."

In response, Applicant has the following observations:

B.1. Patent Application References to Different Forms of the Contour Resistor:

In response to the Examiners charge of applicant not providing any design or fabrication details or illustrations, the Examiner is respectfully again referred to the discussion in section A above.

B.2. Filament, Packing and Conductive Material Description

(page 10 lines 8 – 16) *Such a resistor can comprise a contour resistor which contacts the fluid within the channel by forming a part of the channel wall, or the continuously varying resistor can comprise a filament within the separation channel, or the continuously varying resistor can comprise some other variable, such as a packing within the separation channel that varies in resistivity as a continuous function of position along the longitudinal axis. In further detail, a contour resistor can comprise a conductive material having a cross sectional*

shape which varies as a continuous function of position along the longitudinal axis. Alternatively, the contour resistor can be configured so that it has a material property that varies as a continuous function of position along said longitudinal axis.

(page 17 line 22 to page 18 lines 1- 7) {The references are to figure5} *For example in a channel 60 of circular cross section a filament 62 of non-conductive material can be disposed within, and comprise a section 64 comprising a shunt resistor in fluid contact with the interior of the channel and having a variable which is a continuous function of position along the longitudinal axis of the channel.* ***This can be done for example by variation of material 66 deposited on the filament, or varying the diameter of the filament in the shunt resistor segment to form a reduced diameter section 68 as well as varying the thickness of deposited material. Other ways of varying the resistance within a segment of a channel of round, rectilinear, or other cross-sectional shape are possible.***

The concept, meaning, and description of specific examples of devices characterizable as a "contour resister" are given and are clear from the disclosure. The rejection must be withdrawn or clarified in light of the foregoing.

C. Concerning "Generators"

The Examiner has stated:

" The written description discloses four electrical systems: 1) a continuous electric field intensity generator, 2) an electroosmotic flow generator, 3) a first orientation electric field generator (optional), 4) a second [field] orientation electric field generator (optional). The disclosure of the last two is inadequate for the following

reasons. The structure of the first orientation field generator is the same as one possible structure for the electroosmotic generator. This raises the question, i.e. how is the first orientation electric field generator different from the electroosmotic flow generator? The second orientation electric field generator is only described in terms of desired results. In addition, the limited disclosures of the first orientation electric field generator and the second orientation electric field generator are in isolation, i.e. no disclosure of structural relationships to other elements. Hence, there is no disclosure of embodiments comprising the combination of a continuous electric field intensity generator, an electroosmotic flow generator, and a first orientation electric field generator or the combination of a continuous electric field orientation generator and a second electric field generator."

Concerning patent application references to the first and second electric field generator:

C.1. First orientation electric field generator description

(page 11 lines 7 - 12) *In another detailed aspect, the system can further comprise a first orientation electric field generator. The first orientation electric field generator can comprise an electroosmotic flow generator as set forth above,* *wherein the first-plate and the second plate are brought to different potentials so as to create a transverse or alignment electric field configured to align bipolar molecules in directions normal to the first and second plates.* *The orientation electric field can be made to oscillate at a selected frequency.*

(page 23 lines 18- 22) [figure 9] *An inherent advantage of this configuration is that* *by applying a different potential to the upper control surface 83 than the lower surface 85,* *a*

transverse, or "orientation," electric field can be produced which tends to orient polar molecules (such as proteins and DNA fragments) more uniformly. This makes it possible to have a further tool in separation as it makes it so that differences in mobility due to geometry and size are accentuated.

C.2. First orientation electric field generator description relative to other channel components

(page 20 line 7 to page 21 line 2) [figures 6, 7, 8] The first, or primary separation channel 32 is formed between two layers 70, 72 of a deposited material having a high dielectric constant. Contour resistors 74,76 and frit material 78 comprise a layer sandwiched between the dielectric layers and define the sides of the first channel. The first channel has a high aspect ratio rectangular cross section (50 μm x 4000 μm) that forms a continuous 18 cm long enclosed primary channel containing an electrolyte. The shape provides good EOF bulk flow and heat transfer characteristics due to the small size in one dimension, but allows greater fluid volume due to the large size in the other dimension. One end of the channel terminates into a reservoir of buffer solution (not shown) with an upper electrode (+/- high voltage supply), while the other end of the passage terminates into a reservoir of buffer solution that is at ground potential (lower electrode). In the illustrated embodiment, an anode 80 is connected to a power source 18 and the cathode is at ground potential. An analyte sample is injected into the primary channel via a small passage (sample port) 82 near the lower electrode (cathode, not shown). The sample will be conveyed by EOF toward the separation portion adjacent the contour resistors 74, 76, where primary separation will occur as discussed above. It is well to note that the contour resistor configuration overcomes an

inherent problem of localized variation in electric field intensity as analyte species concentrate at a location, which tends to un-focus the fluid segments or bands forming, by providing a shunting current path around the fluid segment.

C.3. Second orientation electric field generator description

(page 11 lines 12 – 16) *The system can further comprise a second orientation electric field generator configured for generating a second orientation electric field acting in a direction normal to the first orientation electric field, wherein the first and second orientation electric fields can be varied to orient bipolar molecules to a selected orientation by cooperation between the first and second orientation alignment electric fields.*

(page 28 line 19 to page 29 line 7) *With reference again to FIG. 8, two lateral field electrodes 102, 104 can be placed outboard of the channel 32 and* [~~contour~~] *electrodes 74, 76. These lateral field electrodes enable further fine control of separation of analytes. For example, they can be used to separate like molecules of differing length. As will be appreciated the longer a molecule is, the greater the difference in mobility in a longitudinal direction as compared with mobility in a transverse direction. Also, the longer it is, the more "stiffened" it is generally in the presence of the longitudinal electrical field compared to a normal state. Applying a lateral AC electric field will tend to rotate, or at least "wiggle" polar molecules, and the longer the molecule the more this effect will tend to influence its mobility in a direction parallel with the longitudinal axis of the channel 32 and the EOF induced flow of the electrolyte solution as the frontal area exposed to the flow will be greater.*

(page 29 lines 14 – 19) ... *a second transverse orientation field can be applied to further aid in distinguishing analyte species. With reference to FIG. 8 particularly, lateral field electrodes 102, 104 can be laid down adjacent the channel, but outboard of the contour resistors 74, 76. These further electrodes can be brought to different potentials to further alter molecular orientation. Broadly speaking, they provide one more control parameter that can be adjusted to enhance system performance.*

The first orientation electric field generator and the electroosmotic flow generator are the same assembly but are operated with different plate voltages. The first orientation electric field generator has its upper and lower control surfaces driven independently of each other, while the electroosmotic flow generator drives these same control surfaces with the same input voltage. Figure 9 and 11 show the elements that make up the basic function. Figures 6, 7 and 8 show the interrelationship of these elements with the other structural elements of the assembly. A preferred fabrication is also given.

The second orientation electric field generator is described by its function as well as its individual elements.

The rejection is unsupported by the facts, and for the reasons set out above must be withdrawn or clarified.

D. Concerning EOF

The Examiner states:

"the function of the electroosmotic generator is unclear. Page 6 of the specification recites, “an electroosmotic flow generator configured to generate an

electroosmotic flow...". Page 8 or the specification, "The electroosmotic flow generator can comprise a first plate disposed adjacent one side of the containment and configured to *alter the zeta potential* on an interior surface of the separation channel adjacent the first side of the containment, and a second plate adjacent a second side of the containment configured *to alter the zeta potential* on the interior surface of the containment [separation channel] adjacent the second side of the containment. How can the same element of the invention have two different functions? The latter function is consistent with the prior art. However, if the latter function is correct then calling this element an electroosmotic flow generator is repugnant to the normal meaning of "generator". On page 23 the specification recites, "two lateral field electrodes" and contour electrodes". From fig. 8 it looks like "contour electrodes 74, 76" are the same element as contour resistors. What are these elements? Resistors or electrodes? What term(s) in the claims if any correspond to the "lateral field electrodes"? There is some description of the analyte concentrator. However, the analyte concentrator is illustrated as a black box. Such illustration is permitted only if the analyte concentrator is an "off-the shelf" device. See Ex Sziklai. 110 USPQ 325"

In answer to these concerns raised, the Applicant has the following observations:

D.1. Electroosmotic flow generator definition:

(page 8 line 21 to page 9 line 10) ... *an electroosmotic flow generator configured to generate an electroosmotic flow along the longitudinal axis of the separation channel, which electroosmotic flow is variable as to at least one of: (i) the magnitude of the flow,*

and (ii) the direction of the flow, to enhance separation of said at least one analyte species by enabling control of an interaction of forces acting on it created by the continuous electric field intensity gradient generator and the electroosmotic flow generator.

In a more detailed aspect, such a system can be provided wherein the electroosmotic flow generator comprises a power supply and a distributed source of potential positioned adjacent said containment on an exterior surface. As a result, the zeta potential of an interior surface in fluid contact with the separation channel can be altered by at least one of: a) applying a potential, and b) altering at least one of: (i)the magnitude, and (ii) polarity, of potential applied, to the distributed source of potential from the power supply.

D.2. Physical Description and operation of the electroosmotic flow generator

(page 21 line 17 to page 23 line 17) *Along the 4000 μm upper and lower sides of the channel, the channel is defined by the top and bottom dielectric layer 70, 72. Each is about 125 μm thick and formed of a dielectric material comprising ceramic loaded titanate having a permittivity of about 3.00×10^{-9} F/m). Each in turn has a distributed resistor 84, 86 laminated to its surface on a side opposite of the first channel 32. Thus, two plane parallel capacitors are formed on opposite sides of the channel with the buffer acting as the common conductor and the two distributed resistors each acting as the second conductor for each capacitor. These distributed resistors cooperate with the dielectric layers and buffer (electrolyte) solution to form a second electric field generator or electroosmotic flow generator adapted to provide fine control of EOF-induced bulk*

flow.

This can be more readily visualized with reference to FIG. 9, wherein like reference numbers refer to like elements, though not necessarily identical elements (as they do throughout this disclosure). Control surfaces 83, 85 on the dielectric layers 70, 72 have variable zeta potentials due to the distributed resistors 84, 86 deposited on the opposite sides of the respective dielectric layers. The use of an external voltage to control the zeta potential of a capillary was first proposed by Blanchard and Lee as discussed above. Since then, several other researchers have disclosed other variations of this method. However, all of these references disclose conventional capillaries and rely on fused silica as the structural material, resulting in a small bound charge being impressed on the bore. In the Blanchard and Lee patent, an applied voltage of 6,000 V across the wall of a fused silica capillary was barely able to reverse the EOF because the bound charge generated at the inner surface of the bore appears to be only about 0.21 μcoulombs (estimated). Since fused silica has a low dielectric constant (4.2) and has a very active surface, the voltage required to reverse the EOF was very large. However, by reducing the surface activity of the wall, decreasing the wall thickness, and increasing the dielectric constant, a much lower voltage may be used to effect large changes in the EOF, including a polarity reversal.

The thick film distributed resistors 84,86 and the low surface activity dielectric layers 70,72 each form the equivalent of a planar capacitor with the electrolyte solution in the channel 32 and have a capacitance that is determined by the following equation:

$$C = A\varepsilon/L$$

where A is the area (18 cm x 4000 μm), ε is the permittivity of ceramic loaded titanate (ε

= 3000 x 10^{-12} F/m), L is the thickness in meters (125 μm), and C is the capacitance in farads © = 17.3 nF). Once the capacitance is known, the bound charge at the interface can be calculated as follows:

$$q = CV$$

where q is in coulombs. For V = 100 volts, q = 1.73 μ coulombs. Early attempts to alter the EOF of a capillary by an external voltage were not practical because the applied voltage varied significantly over the length of the capillary, resulting in an apparent velocity that was not predictable. Since the electrolyte voltage linearly decreases along the length of the channel, the control surfaces must follow the same profile, but be offset by a fixed amount in order to obtain a constant EOF along the channel length. This requires that each control surface 83, 85 have floating voltage sources 88, 90, 92, 94 at both the anode and cathode ends of its distributed resistor. These are digitally controlled by a microprocessor-based controller (not shown) such as a computer interfaced to an isolated D/A converter and high voltage amplifier. This interface is through an optical isolator of conventional configuration or an optical waveguide connected to a transmitter and receiver.

D.3. Lateral Field Electrode Location and Definition

(page 28 lines 19 – 21) *With reference again to FIG. 8, two lateral field electrodes 102, 104 can be placed outboard of the channel 32 and [~~contour~~] electrodes 74, 76. These lateral field electrodes enable further fine control of separation of analytes.*

(page 29 lines 15 – 19) *With reference to FIG. 8 particularly, lateral field electrodes 102, 104 can be laid down adjacent the channel, but outboard of the contour resistors 74, 76. These further electrodes can be brought to different potentials to further alter molecular orientation. Broadly speaking, they provide one more control parameter that can be adjusted to enhance system performance.*

D.4. Analyte Concentrator Description

(page 44 lines 2 – 5) (figure 14) ... *the analyte concentrator comprises first 174 and second 176 electrodes connected to an isolated ground 178 and the output of an operational amplifier 180 connected to an interface with the computer comprising a controller (not shown), for example by means of a digital/analog converter 182 .*

It is well known in capillary electrophoresis that electroosmotic flow is related (proportional) to zeta potential. Changing the voltage on the distributed resistors 84, 86 (FIG. 9) results in the zeta potential of the interior surfaces of the channel to change, which in turn changes the electroosmotic flow of the channel. Since the end result of applying the same voltage to both control surfaces is a change in electroosmotic flow it would appear reasonable to define the assembly as an electroosmotic flow generator. The physical process by which this occurs is described in the disclosure as pointed out in section E.2. above. The electroosmotic flow generator is also defined functionally in the disclosure, as pointed out in section E.1 above.

As mentioned, the term "*contour electrode*" is in error and instead should be just "electrode" per the amended specification paragraph set forth above. These electrodes are used

to induce a lateral field within the channel and provide additional fine control in the separation, as discussed in the disclosure. See section E.3 above in this regard.

The elements that make up the analyte concentrator are described in the disclosure as discussed above in section E.3, and are graphically depicted in figure 14. The analyte concentrator consists of two separated electrodes that are lateral to the channel and driven by an isolated operational amplifier as shown in figure 14. The two electrodes are designated 174 and 176. The written description sets out all that is needed to practice this aspect, as discussed in section E.4. above.

III. The Disclosure of the Application is Enabling to one Skilled in the Art.

The application is enabling to one engaged in constructing a device of this kind. In support of this statement, please again refer to the Declaration of David Le Febre, with Exhibits, attached.

IV. Conclusion re 112 1st paragraph rejections

For at least the foregoing reasons, these rejections under Section 112 first paragraph are without merit. These rejections must be withdrawn or clarified so that Applicant can respond.

Rejections under 35 U.S.C. Section 112, Second Paragraph

Claims 1-56 stand rejected under 35 U.S.C. § 112, second paragraph, as indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

I. Discussion Of Specific Concerns Enunciated In The Rejection

A. Re EOF: The first concern raised, concerning Claim 1 is not understood. Claim 1 appears to be rejected for indefiniteness because the Examiner does not appreciate that altering the zeta potential is not only <u>not</u> inconsistent with, but is part and parcel of "generating" (consistent with the Examiner's definition of "generating" at the top of p.7 of the Office Action) an electroosmotic bulk flow in the channel. Applicant commends to the Examiner consultation of any of the number of good reference works on the subject, for example Wehr, et al. **Capillary Electrophoresis of Proteins, Marcel Dekker, Inc. New York 1999.** Further, review of the Ivory reference cited against the application will be instructive on this point, particularly at cols. 17-20.

As discussed above, the specification teaches that some structure fills more than one role. That is the case here. As discussed above, the specification teaches what is required for each of the claimed elements. Because structure used for one element set forth in the claim is also used for another does not render the claim indefinite. Here the requirements for support are met for the reasons set forth above. As far as it can be understood then, the rejection does not appear to be grounded in fact, and should be withdrawn.

B. Re Distributed Source of Potential: The rejection of claim 2 is not understood. An example in the disclosure illustrates the point, i.e. a plate attached to one leg of the power supply will be understood by those skilled in the art to be a distributed source of potential (distributed over the area of the plate), as opposed to a point source, and beyond that comment Applicant does not know how to respond to the rejection, as the meaning of the term will be apparent to practitioners in the art.

C. Regarding the Examiner's suggestion with regard to Claim 3, this is not understood. If anything, the language might be changed to "comprises" but the Examiner's suggestion would not result in a properly constructed sentence in English.

D. Regarding the Examiner's concerns with regard to claim 4, these are well taken. The apparent double inclusion was the result of a typographical error, and the concerns are obviated by the change in dependency of claim 4 from claim 3 to claim 2.

E. Re Contour Resistors: Regarding the concerns about claims 5 and 6, these are not understood. Per the above discussion a contour resistor can be provided in many forms, including as a filamentary element or a packing within a separation channel.

F. Dependency of claims 7 and 8 has been corrected. The correction obviates the concerns raised regarding these claims.

G. Regarding claim 15, the rejection is not understood. Altering the zeta potential is not inconsistent with generating flow, as discussed above. This is an additional function, not a "different" function, and the rejection should be withdrawn.

H. The rejection of claims 16 and 43 are not understood, and appears to be based on in/mis-comprehension of certain relevant facts, as discussed above and for the reasons set forth above concerning the elements of these claims the Examiner mentions.

I. The Examiner's concerns with regard to claims 17 and 44, insofar as understood (the same structure being capable of more than one function) have been addressed above. Reiterating briefly for full response, the two elements set forth in the claims, which perform different functions, can share one, two, or more, physical elements in common as embodied in the example device disclosed. It is both possible and desirable in embodiments where

simplicity and low cost are goals to have physical elements perform multiple roles. The Examiner's implication that the elegance of the example embodiment may render the claim indefinite because one or more elements perform more than one function is both puzzling and troubling to the Applicant.

J. The Examiner's concerns regarding claims 21, 26, 47, 52, 53, (specifically that a "a second" without "a first" is set forth) while not rendering the claim unpatentable, point to a formal matter involving U.S. patent practice convention, and these have been addressed by amendment of the claims, as set forth above.

K. The concerns expressed regarding claims 18, 27, and 44 are not understood. The Examiner has not established that the claims from which these claims depend do not structurally distinguish over the prior art. The fact that a dependent claim sets forth only a functional limitation does not, of itself, render the claim unpatentable under Section 112 second paragraph. (See, *e.g.* MPEP Sec. 2173.05(g).)

L. The concerns regarding claim 28 and 41 have been addressed by the amendments set forth above.

M. The concerns regarding claims 43 and 44 are not understood for the same reasons the rejections of claims 16 and 17 are not understood, as set out above.

N. The concerns regarding claim 45 are not understood. The relationships are set out in the disclosure, for at least the reasons set forth above. Further all the elements in the claim are set out in the disclosure, for at least the reasons set forth above.

O. The concerns regarding claims 50 and 56 are not understood, from the disclosure it is clear that they could, in different circumstances, be included in other elements, or can be stand-alone. Again, that the same structure can perform different functions, even at the same

time, doesn't render the claims unpatentable. The Applicant is not to be punished for disclosing an elegant and simple solution to a problem.

P. The formal rejections of the other claims should be withdrawn for the same reasons set forth concerning the claims from which they depend.

II. Conclusion

The claims are definite for the reasons set forth above. The rejections should be withdrawn for at least these reasons.

Claim Rejections - 35 U.S.C. § 102

Claims 1,2,9,10, and 11 (including independent claim 1) were rejected under 35 U.S.C. § 102(b) as being anticipated by Ivory, et al. This rejection is either specious or is not understood by Applicant. Applicant assumes the later as the Examiner assisted in Examining the cited reference. The Ivory reference does not teach or suggest the element of:

> "a first separation channel defined by a confinement enclosing an interior channel volume, said first separation channel having first and second ends and a longitudinal axis, and said first separation channel being configured to contain an electrolyte solution within the interior channel volume, said separation channel providing the only flowpath for both the analyte sample and the electrolyte solution."

The Ivory reference teaches a device where electrolyte solution can have a different flowpath than the separation channel, and has a flowpath separated from the analyte sample. With reference to FIG. 1 of the Ivory disclosure, the separation chamber 12 is separated from the electrode chamber 14 by the dialysis membrane 16. Electrolyte can flow in the electrode

chamber but analyte (note: not anolyte) cannot. Analyte can only flow in the separation channel. The reference teaches not only different flowpaths; but it teaches that, at least in the example embodiment, it is preferable to have the direction of sample flow in the electrode chamber reversed from the direction of flow in the separation chamber (see, e.g. col. 9, lines 27-33). Therefore, for at least these reasons this element of the claim is not met in the cited reference.

The rejected claims dependent on claim 1, being more narrow in scope, are allowable for the same reason claim 1 is allowable. For at least these reasons, the rejection of these claims must be withdrawn.

CONCLUSION

In light of the above, Applicant respectfully submits that pending claims 1-62 are in condition for allowance. Applicant has amended the application to address the formal matters raised by the Examiner. These amendments were not made for reasons related to patentability, but go only to the formal matters raised. The Claims are patentable as to matters of substance for the reasons set forth above. Therefore, Applicant requests that the rejections and objections be withdrawn, and that the claims be allowed and passed to issue.

Check No. 17358, in the amount of $55.00, is enclosed pursuant to 37 C.F.R. § 1.17(a), for a 1 month extension of time pursuant to 37 C.F.R. § 1.136, extending the shortened statutory period for response to July 11, 2003. No new claims were added. Therefore, no additional fee is due.

The Commissioner is hereby authorized to charge any additional fee or to credit any overpayment in connection with this Amendment to Deposit Account No. 20-0100.

DATED this 11th day of July, 2003.

Respectfully submitted,

Clifton W. Thompson
Registration No. 36, 947

THORPE, NORTH & WESTERN, L.L.P.
P.O. Box 1219
Sandy, Utah 84091-1219
Telephone: (801) 566-6633

H:\FILES\T8000\T8526\Amendment710final.doc